SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Nicotinell Icemint 2mg Medicated Chewing Gum

Nicotinell Support Icemint 2mg medicated Chewing Gum

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One piece of medicated chewing gum contains 2 mg nicotine (as 10 mg nicotine – polacrilin (1:4)).

For excipients, see section 6.1

3 PHARMACEUTICAL FORM

Medicated chewing gum.

Each piece of coated chewing gum is off-white in colour and rectangular in shape.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Nicotinell gum relieves and/or prevents craving and nicotine withdrawal symptoms associated with tobacco dependence. It is indicated to aid smokers wishing to quit or reduce prior to quitting, to assist smokers who are unwilling or unable to smoke, and as a safer alternative to smoking for smokers and those around them.

Nicotinell gum is indicated in pregnant and lactating women making a quit attempt.

Nicotinell gum should preferably be used in conjunction with a behavioural support programme.

4.2 Posology and method of administration

Posology

Adults over 18 years of age and the elderly

The 2 mg chewing gum is recommended in smokers with a low to moderate nicotine dependency.

The 2 mg chewing gum may not be well suited to smokers with a strong or very strong nicotine dependency.

The optimal dosage form is selected according to the following table:

Low to moderate dependency	Moderate to strong dependency	Strong to very strong dependency
Less than 20 cigarettes / day	From 20 to 30 cigarettes / day	Over 30 cigarettes / day
Low dose forms are preferable (2 mg gum)	Low (2 mg gum) or high (4 mg gum) dose forms are acceptable depending on patient characteristics and preference.	High dose forms are preferable (4 mg gum)

Low dosage forms acceptable

High dosage forms acceptable

If an adverse event is noted when high dose forms are initiated, this should be replaced by the lower dosage form.

One piece of Nicotinell gum to be chewed when the user feels the urge to smoke. Do not use more than 1 gum per hour. Normally, 8-12 pieces per day can be used, up to a maximum of 24 pieces per day.

The characteristics of chewing-gum as a pharmaceutical form are such that individually different nicotine levels can result in the blood. Therefore, dosage frequency should be adjusted according to individual requirements within the stated maximum limit.

The treatment time is individual. Normally, treatment should continue for at least 3 months.

After three months, the user should gradually cut down the number of pieces chewed each day until they have stopped using the product.

Treatment should be discontinued when the dose has been reduced to 1-2 pieces of gum per day.

Nicotine gum should not be used for more than 12 months unless the potential benefit outweighs the potential risk to the smokers.

Nicotinell gum is sugar free.

Children and Adolescents (aged 12-17 years of age)

The above recommendation can be used for adolescents aged between 12 and 17 years of age. As data are limited in this age group, medical advice should be obtained should it be found necessary to use the gum beyond 12 weeks. The use of NRT in adolescents should only be used when the benefits of abstinence outweigh the risks of continued smoking. Nicotine gum should preferably be used in conjunction with a behavioural support programme as this normally improves the success rate.

Adolescents should not quit with a combination NRT Regimen.

Children below 12 years of age

Nicotine gum are not recommended for use in children under 12 years.

Hepatic and Renal Impairment

Use with caution in patients with moderate to severe renal impairment as the clearance of nicotine or its metabolites may be decreased with the potential for increased adverse effects (see section 4.4).

Concomitant use of acidic beverages such as coffee or soda may decrease the buccal absorption of nicotine. Acidic beverages should be avoided for 15 minutes prior to chewing the gum.

Method of administration

1. One piece of gum should be chewed until the taste becomes strong.
2. The chewing gum should be rested between the gum and cheek.
3. When the taste fades, chewing should commence again.
4. The chewing routine should be repeated for 30 minutes.

4.3 Contraindications

Hypersensitivity to nicotine or any components of the gum listed in section 6.1.

Nicotinell gum should not be used by non-smokers or occasional smokers.

4.4 Special warnings and precautions for use

Any risks that may be associated with nicotine replacement therapy are substantially

outweighed by the well established dangers of continued smoking.

Precautions
Users should be informed that if they continue to smoke while using the gums they may experience increased adverse effects due to the hazards of smoking, including cardiovascular effects.

Cardiovascular disease
In stable cardiovascular disease Nicotinell gum presents a lesser hazard than continuing to smoke. However dependant smokers currently hospitalised as a result of a recent myocardial infarction, unstable or worsening angina including Prinzmetal's angina, severe cardiac arrhythmias, uncontrolled hypertension, or recent cerebrovascular accident who are considered to be haemodynamically unstable should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). If this fails, Nicotinell gum may be considered but as data on safety in this patient group are limited, initiation should only be under medical supervision. If there is a clinicallysignificant increase in cardiovascular or other effects attributable to nicotine, the nicotine gum dose should be reduced or discontinued.

Diabetes mellitus
Patients with diabetes mellitus should be advised to monitor their blood sugar levels more closely than usual when nicotine replacement therapy is initiated as catecholamines released by nicotine can affect carbohydrate metabolism.

Allergic reactions
Angioedema and urticaria have been reported.

Gastro-intestinal disease
Swallowed nicotine may exacerbate symptoms in patients suffering from active oesophagitis, oral or pharyngeal inflammation, gastritis, or peptic ulcers and oral nicotine replacement therapy preparations should be used with caution in these conditions. Ulcerative stomatitis has been reported.

Renal and or hepatic impairment
Should be used with caution in patients with moderate to severe hepatic impairment and/or severe renal impairment as the clearance of nicotine or its metabolites may be decreased with the potential for increased adverse effects.

Seizures
Use with caution in subjects taking anti-convulsant therapy or with a history of epilepsy as cases of convulsions have been reported in association with nicotine.

Danger in small children
Doses of nicotine tolerated by adult and adolescent smokers can produce severe toxicity in small children that may be fatal (please see section 4.9). Products containing nicotine should not be left where they may be misused, handled or ingested by children. Nicotinell gum should be disposed of with care. Nicotine products should be kept out of sight and reach of children.

Phaeochromocytoma and uncontrolled hyperthyroidism

Nicotinell gum should be used with caution in patients with uncontrolled hyperthyroidism or pheochromocytoma as nicotine causes the release of catecholamines.

Transferred dependence
Transferred dependence is rare and is both less harmful and easier to break than smoking dependence.

Stopping smoking
Polycyclic aromatic hydrocarbons in tobacco smoke induce the metabolism of drugs catalysed by CYP 1A2 (and possibly CYP 1A1). When a smoker stops, this may result in slower metabolism and a consequential rise in blood levels of drugs such as theophylline, tacrine, olanzaprine and clozaprine.

Other warnings
People having problems with the joint of the jawbone and denture wearers may experience difficulty in chewing the gum. In this case, it is recommended that they use a different pharmaceutical form of nicotine replacement therapy.

Nicotine gum may loosen fillings or dental implants.

Special warnings about excipients
Because Nicotinell gum contains sorbitol, xylitol and maltitol: Patients with rare hereditary conditions of fructose intolerance should not take this medicine.

Nicotinell Icemint 2 mg coated chewing-gum contains sweetners including sorbitol (E420) 0.2 g per chewing-gum, a source of 0.04 g fructose. Calorific value 1.0 kcal/piece of chewing-gum.

Nicotinell Icemint 2 mg contains less than 1 mmol sodium (23 mg) per chewing gum, that is to say essentially ‘sodium-free’.

The gum base contains butylhydroxytoluene (E321) which may cause local irritation to mucous membranes.

4.5 Interaction with other medicinal products and other forms of interaction

No information is available on interactions between Nicotinell gum and other drugs. No clinically relevant interactions between nicotine replacement therapy and other drugs has definitely been established, however nicotine may possibly enhance the haemodynamic effects of adenosine. Smoking cessation itself may require adjustment of some drug therapy.

4.6 Fertility, pregnancy and lactation

Pregnancy
Adverse reproductive and developmental effects have been reported following exposure to tobacco and nicotine during pregnancy. Women who are pregnant should first be advised to stop smoking without the assistance of nicotine replacement therapy. Stopping smoking is the single most effective intervention for improving the health of both the pregnant smoker and her baby, and the earlier abstinence is achieved the better. However, if the mother cannot (or is considered unlikely to) quit without pharmacological support, NRT may be used

as the risk to the foetus is lower than that expected with smoking tobacco. Stopping completely is by far the best option but Nicotinell gums may be used in pregnancy as a safer alternative to smoking and should only be used if the expected benefits to the mother outweigh the potential risks to the foetus. Because of the potential for nicotine-free periods, intermittent dose forms are preferable, but patches may be necessary if there is significant nausea and/or vomiting. If patches are used they should, if possible, be removed at night when the foetus would not normally be exposed to nicotine.

Lactation

Nicotine is excreted in breast milk. Nicotine replacement therapy should therefore be avoided during breast-feeding. Should smoking withdrawal not be achieved, oral forms of nicotine replacement therapy gum may be considered as intermittent dose forms would minimize the amount of nicotine in breast milk and permit feeding when levels were at their lowest.

However, oral forms of nicotine replacement therapy should only be used if the expected benefits to the nursing mother outweigh the potential risks to the infant. The relatively small amounts of nicotine found in breast milk during NRT use are less hazardous to the infant than second-hand smoke.

Fertility

Smoking increases the risk for infertility in women and men. Both in humans and in animals it has been shown that nicotine can adversely affect sperm quality. In animals, reduced fertility has been shown.

4.7 Effects on ability to drive and use machines

There is no evidence of any risks associated with driving or operating machinery when Nicotinell gum is used following the recommended dose. Nevertheless, one should take into consideration that smoking cessation can cause behavioural changes.

4.8 Undesirable effects

Certain symptoms such as dizziness, headache and sleep disturbances may be related to withdrawal symptoms in connection with smoking cessation and may be due to insufficient administration of nicotine. Cold sores may develop in connection with smoking cessation, but any relation with the nicotine treatment is unclear.

Nicotinell gums can cause adverse reactions similar to those associated with nicotine administered by other means (including smoking). These can be attributed to the pharmacological effects of nicotine, which are dose dependant. Non dose-dependent adverse reactions are as follows:

Jaw muscle ache, erythema, urticaria, hypersensitivity,

angioneurotic oedema and anaphylactic reactions.

At recommended doses Nicotinell gum has not been found to cause any serious adverse effects. Excessive consumption of Nicotinell gum by those who have not been in the habit of inhaling tobacco smoke could possibly lead to nausea, faintness or headaches.

Increased frequency of aphthous ulcer may occur after abstinence from smoking.

Most of the side effects which are reported by patients occur generally during the first 3-4 weeks after initiation of therapy.

Nicotine from gums may sometimes cause a slight irritation of the throat and increase salivation at the start of the treatment.

Excessive swallowing of nicotine which is released in the saliva may, at first, cause hiccups. Those who are prone to indigestion may suffer initially from minor degrees of dyspepsia or heartburn; slower chewing will usually overcome this problem.

The gum may stick to and in rare cases damage dentures and dental appliances.

The following undesirable effects detailed in Table 1 are nicotine related adverse events for all oral dosage forms. Table 1 shows events which were identified from a double-blind, randomised, placebo-controlled lozenge clinical study involving 1818 patients. Adverse events reported in this study have been considered for inclusion, where the incidence in the 2 mg or 4 mg nicotine arm was higher than the corresponding placebo arm. Frequencies are calculated from safety data of the study.

Table 1: Adverse Reaction from clinical trial data

Adverse reactions are listed below, by system organ class and frequency.
Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to
<1/100), rare (≥1/10,000 to <1/1,000) or very rare (<1/10,000),

System Organ Class	Adverse Reaction	Frequency
Psychiatric Disorders	Insomnia*	Common
Nervous system disorders	Headache*, dizziness*	Common
	Seizures	Not Known
Gastrointestinal disorders	Salivary hypersecretion, stomatitis, oral pain, oral discomfort, hiccups, nausea, vomiting, dyspepsia**, abdominal pain upper, diarrhoea, dry mouth, constipation and flatulence.	Common
Musculoskeletal, connective and bone disorders	Jaw muscle ache***	Common
Cardiac disorders	Palpitations	Uncommon
	Atrial arrhythmia	Rare
Skin and subcutaneous tissue disorders	Erythema, urticaria	Uncommon
Immune system disorders	Hypersensitivity, angioneurotic oedema and anaphylactic reactions.	Rare
Respiratory, Thoracic and Mediastinal Disorders	Pharyngitis, cough*, pharyngolaryngeal pain	Common

* These events may also be due to withdrawal symptoms following smoking cessation.

** Individuals with a tendency to experience indigestion may suffer initially from

minor degrees of indigestion or heartburn if the 4 mg dose is used - slower chewing in the case of

gum or the use of the 2 mg dose (if necessary more frequently) will usually overcome this problem.

*** This adverse event could be due to mechanical stress caused by chewing of the gum rather than due to the direct action of nicotine.

Post Marketing Data

Table 2 shows events which were identified from post-marketing experience of nicotine oral forms. As these reactions are reported voluntarily from a population of uncertain size, the frequency of these reactions is unknown.

Table 2: Adverse Reactions from post-marketing data

System Organ Class	Adverse Reaction
Immune system disorders	Hypersensitivity, angioedema, urticaria, ulcerative stomatitis, angioneurotic oedema and very rare anaphylactic reactions.
Nervous system disorders	Tremor
Cardiac disorders	Palpitations, tachycardia, arrhythmias.
Respiratory, Thoracic and Mediastinal Disorders	Dyspnoea
Gastrointestinal Disorders	Dysphagia, eructation, salivary hypersecretion.
General Disorders and Administration Site Conditions	Asthenia****, fatigue****, malaise****, influenza type illness****

**** These events may also be due to withdrawal symptoms following smoking cessation. The patient may still experience nicotine dependence after smoking cessation.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reaction via the Yellow Card Scheme at: www.mhra/gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

In overdose, symptoms corresponding to heavy smoking may be seen, however the toxicity of nicotine cannot be directly compared with that of smoking, because tobacco smoke contains additional toxic substances (e.g. carbon monoxide and tar).

Overdose with Nicotinell gum may only occur if many pieces are chewed simultaneously. Nicotine toxicity after ingestion will most likely be minimized as a result of early nausea and vomiting that occur following excessive nicotine exposure. Risk of poisoning by swallowing the gum is small. Since the release of nicotine from

the gum is slow, very little nicotine is absorbed from the stomach and intestine, and if any is, it will be inactivated in the liver.

Chronic smokers can tolerate doses of nicotine that, in a non-smoker, would be more toxic, because of the development of tolerance.

Even small quantities of nicotine are dangerous in children, and may result in severe symptoms of poisoning which may prove fatal. If poisoning is suspected in a child, a doctor must be consulted immediately.

Symptoms and Signs

Symptoms and signs of an overdose from nicotine gum would be expected to be the same as those of acute nicotine poisoning include pallor, hyperdidrosis, nausea, vomiting, salivation, throat burn, abdominal pain, diarrhoea, perspiration, headache, dizziness, hearing and visual disturbances, tremor, confusional state and marked weakness. In extreme cases, these symptoms may be followed by hypotension, tachycardia, cardiac arrhythmia, dyspnoea, prostration, circulatory collapse, coma and terminal convulsions.

Treatment of overdose

Treatment of overdose should be immediate as symptoms may develop rapidly (particularly in children). All nicotine intake should stop immediately. Emesis is usually spontaneous. Artificial respiration with oxygen should be instituted if necessary. Monitor vital signs and treat symptomatically.

Toxicity

Nicotine is highly toxic by ingestion, inhalation and skin contact. The fatal dose has been estimated to be as little as 40 mg of nicotine in an adult and just a few milligrams of nicotine have caused severe symptoms. It can be very rapidly absorbed with CNS, neuromuscular and autonomic features. The half-life of nicotine ranges from 24 minutes to 2 hours but symptoms may persist for up to 72 hours in severe cases of poisoning.

- All patients who have taken a deliberate overdose should be referred for assessment.
- Children and adults who have ingested 0.2 mg/kg or more nicotine, or those who are symptomatic, should be referred for medical assessment.
- Children or adults who have accidentally ingested less than 0.2 mg/kg nicotine and who have no new symptoms since the time of ingestion do not need to be referred for medical assessment. Patients should be advised to seek medical attention if symptoms develop.
- All symptomatic children and adults following accidental transdermal patch application should be referred for medical assessment.

Features

- Early features of ingestion include burning in the mouth and throat, nausea, vomiting, confusion, dizziness, weakness, hypersalivation, sweating and increased bronchial secretions. There may be sympathetic features including tachycardia, tachypnoea, hypertension and agitation followed by bradycardia, systemic hypotension and respiratory depression.
- More severe poisoning leads to arrhythmias including atrial fibrillation, coma, convulsions and respiratory and cardiac arrest. Recovery is likely if survival exceeds 2-3 hours.

- Skin contact may lead to irritation followed by variable absorption depending on the length of exposure and concentration. Systemic features may follow.
- Eye contact with liquid may lead to irritation and lacrimation.

Management

General measures

- Maintain a clear airway/ensure adequate ventilation. Monitor pulse and BP. Perform 12 lead ECG and measure QRS duration and QT interval and repeat especially if the patient is symptomatic or has taken slow release preparations
- Good neurological outcome after cardiac arrest (due to nicotine poisoning) may occur after prolonged resuscitation. Cardiac arrest in hospital or witnessed out of hospital, with bystander CPR, should be continued for at least 1 hour (discuss with local poisons centre)
- The benefits of gastric decontamination are uncertain. Consider activated charcoal (50g adults: 1g/kg children) provided airway can be protected in those presenting within 1 hour of ingestion of more than 0.2mg/kg of nicotine.
- Asymptomatic patients who have ingested more than 0.2mg/kg of nicotine should be observed for at least 4 hours. However, if other cardiac/cardiotoxic agents have been taken monitor for the longest period recommended for these.
- In symptomatic patients check U&Es, creatinine kinase and arterial blood gases.
- Contact the local poisons information centre (UK – NPIS: Ireland - NPIC) for specific advice

Bradycardia

- If symptomatic give IV atropine
- If associated with hypotension, dobutamine or isoprenaline may be considered
- Temporary pacemaker or external pacing may be required

Agitation

- Agitated adults can be sedated (IV diazepam: if ineffective oral or parenteral haloperidol)
- Agitated children are better managed without sedation. Exclude other causes (e.g. hypoxia: infection: hypoglycaemia: raised ICP). Seek expert paediatric advice

Hypertension

- Adults: in agitated patient hypertension may settle with sedation. If hypertension persists give IV nitrates until blood pressure controlled. Calcium antagonists are an alternative as second line therapy. Phentolamine or sodium nitroprusside are options if there is hypertension without evidence of cardiac ischaemia (but may cause a rapid fall in blood pressure) or alternatively IV labetalol.
- Children (under 5 years): Seek expert paediatric advice

Convulsions

- Give oxygen, check blood sugar, U&Es and arterial blood gases. Correct acid-base balance and metabolic disturbances as necessary
- A single brief convulsion does not require treatment. Otherwise control with IV diazepam or lorazepam. If unresponsive seek advice from NPIS/NPIC or appropriate specialist

Other points to note

- A high percentage of urine screens will be positive for nicotine in both smokers and non-smokers
- Quantitative blood concentrations are not readily available. Appropriate history and recognition of clinical finding are important
- Other treatments/measures indicated by patient's clinical condition
- On discharge patients should be advised to seek medical attention if symptoms develop

Skin exposure

- Remove soiled clothes, nicotine patches or contaminating fluid
- Wash skin with soap and water
- Treat symptoms of systemic toxicity as above.

Contact the local poisons information centre (UK – National poisons information service, NPIS) for specific advice.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N07B A01
Pharmacotherapeutic group: Drugs used in nicotine dependence

Nicotine, the primary alkaloid in tobacco products and a naturally occurring autonomous substance, is a nicotine receptor agonist in the peripheral and central nervous systems and has pronounced CNS and cardiovascular effects. On consumption of tobacco products, nicotine has proven to be addictive, resulting in craving and other withdrawal symptoms when administration is stopped. Clinical studies have shown that nicotine replacement products can help smokers abstain from smoking by relieving these withdrawal symptoms. This craving and these withdrawal symptoms include a strong urge to smoke, dysphoria, insomnia, irritability, frustration or anger, anxiety, concentration difficulties agitation and increased appetite or weight gain. Increased appetite is a recognised symptom of nicotine withdrawal and post-cessation weight gain is common. Clinical trials have demonstrated that Nicotine Replacement Therapy can help control weight following a quit attempt. The gum replaces part of the nicotine that would have been administrated via tobacco and reduces the intensity of the withdrawal symptoms and smoking urge.

The gum contains a number of ingredients that are recognized as having properties for removal of dental staining. Studies have shown that the gum helps to improve tooth whiteness.

5.2 Pharmacokinetic properties

When the gum is chewed, nicotine is steadily released into the mouth and is rapidly absorbed through the buccal mucosa. A proportion, by the swallowing of nicotine containing saliva, reaches the stomach and intestine where it is inactivated.

The nicotine peak plasma mean concentration after a single dose of the 2 mg coated gum is approximately 6.4 nanograms per ml (after 45 minutes) (average plasma concentration of nicotine when smoking a cigarette is 15-30 nanograms per ml).

Nicotine is eliminated mainly via hepatic metabolism; small amounts of nicotine are eliminated in unchanged form via the kidneys. The plasma half-life is approximately three hours. Nicotine crosses the blood-brain barrier, the placenta and is detectable in breast milk.

5.3 Preclinical safety data

No definite conclusion can be drawn on the genotoxic activity of nicotine in vitro. Nicotine was negative in in-vivo tests.

Animal experiments have shown that nicotine induces post-implantation loss and reduces the growth of foetuses.

The results of carcinogenicity assays did not provide any clear evidence of a tumorigenic effect of nicotine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gum base (containing butylhydroxytoluene (E321))
Calcium carbonate (E170)
Sorbitol (E420)
Sodium carbonate anhydrous
Sodium hydrogen carbonate (E500)
Polacrilin
Glycerol (E422)
Purified water
Levomenthol
Natural mint flavouring
Mint millicaps
Sucralose (E955)
Acesulfame potassium (E950)
Xylitol (E967)

Mannitol (E421)
Gelatin
Titanium dioxide (E171)
Carnauba wax (E903)
Talc (E553b)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The chewing-gum is packed in PVC/PVdC/aluminium blisters each containing either 2 or 12 pieces of gum. The blisters are packed in boxes containing 2, 12, 24, 36, 48, 60, 72, 84, 96 108, 120 and 204 pieces of gum.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Haleon UK Trading Limited

The Heights
Weybridge
Surrey
KT13 0NY
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 44673/0120

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21/11/2024

10 DATE OF REVISION OF THE TEXT

21/11/2024